

REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.116, are respectfully requested in light of the remarks which follow.

I. Amendments to the Claims

By the foregoing amendments to the claims, claim 1 has been amended, and claim 2 has been canceled.

In particular, claim 1 has been amended to recite the subject matter formerly recited in claim 2. In addition, claim 1 has been further amended to clarify the claim language, for consistency, and to bring the claims into better conformance with U.S. patent practice. These clarifying amendments are merely editorial in nature and are not intended to change the scope of the claims or any elements recited therein.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter canceled or recited herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No Previously Presented matter has been added, and entry of the foregoing amendments of the above-identified application is respectfully requested.

II. Response to Claim Rejections Under 35 U.S.C. § 102

At pages 2-4 of the Office Action, claims 1, 4, 7, 10, and 21 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Kuehnle (U.S. Patent No. 5,516,670). This rejection is respectfully traversed.

To expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, the claims have been amended as described above. In particular, claim 1 has been amended to include the subject matter of claim 2. Because claim 2 has not been included in the 35 U.S.C. § 102 rejection over Kuehnle, the amendments to the claims should be sufficient to overcome this rejection. Accordingly, and Applicants respectfully request reconsideration and withdrawal of this rejection.

III. Response to Claim Rejections Under 35 U.S.C. § 103(a)

A. At pages 4-5 of the Office Action, claims 1-4, 7, 9, 10, 12, 13, 16, 18, 19, 21 and 22 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Kuehnle in view of Hernandez et al. (Microbiology, 1995). This rejection is respectfully traversed.

The present claims are directed to a method for introducing exogenic bioparticles into biological membrane-enveloped structures (e.g. cells) comprising preparing a sample comprising biological membrane-enveloped structures, magnetically susceptible particles and exogenic bioparticles, and applying a magnetic alternating field to said sample, whereby an increase in the thermal energy of said magnetically susceptible particles causes the formation of pores in said biological membrane-enveloped structures (see claim 1).

Kuehnle discloses a method for introducing a reagent, for example genetic material (DNA), into cell or tissue specimens by using magnetic particles of an acicular shape. The magnetic particles are deposited on the surface of the specimen placed close to the focal point of a gradient (nonuniform) magnetic field. Then, the specimen is exposed to the gradient magnetic field. The particles align themselves with the direction of the magnetic field and move towards the specimen, penetrating the cell membrane and if necessary cell walls. As noted at column 6, lines 51-56 of the reference, "[i]n response to the magnetic field, the coated particles align themselves with the field lines and propagate toward the nucleus when the particles encounter the cell's outer membrane, because of their needle-like shape and the force produced by the field . . ." Once the magnetic field is disconnected, the particles stop moving and stay within the cell target. If the particles are coated with a molecule (e.g. DNA) the molecule will enter the specimen together with the particle. However, in contrast to the present claims, the magnetic field involved in transporting the particles (and thus the DNA) into the specimen is not an alternating magnetic field.

Kuehnle does in fact describe an alternating magnetic field (see column 7, lines 9-13). However, it is clear that the alternating magnetic field mentioned in the reference is not relevant to poration of the specimen or the resultant introduction of exogenic bioparticles into the specimen. Instead, Kuehnle teaches that the alternating magnetic field can be used to manipulate coated particles already located in the specimen (see column 6, lines 58-64 ("Once the coated particles reach the cell nucleus, [the] coil may be de-energized so that the particles remain there . . . the presence of the particles at the target site can be observed by

microscopy . . .") and column 7, lines 9-10 ("Once the particles are in the target area, they can be manipulated in situ [using an alternating magnetic field]"). In other words, the alternating magnetic field is not applied until after the magnetic particles have been transported into the cell.

Applicants further submit that Example 4 of the reference, similar to column 7, lines 9-13, demonstrates oscillation of particles once the particles are already in place within the target (i.e. once the particles have traversed the barrier made up by the cellular membrane). Example 4 does not relate to using an alternating magnetic field to introduce exogenic bioparticles into biological membrane-enveloped structures.

In addition, Hernandez et al. does not remedy the serious deficiencies of Kuehnle. Hernandez et al. describes inducing lysis by heat in *E. coli*, showing that cells near the process of cell division are more sensitive to heat. Hernandez et al. do not describe a process wherein temporary pores are created in lipid membranes using local heating of membranes, particularly not local heating due to oscillation of magnetically susceptible particles.

Applicants respectfully submit that the cited references do not teach or suggest the subject matter of the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

B. At pages 5-7 of the Office Action, claims 1-4, 7, 9, 10, 12, 13, 16, 18, 19, 21 and 22 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Pope et al. (Nucleic Acids Research, 1996) in view of Jordan et al. (Int. J. Hyperthermia, 1993). This rejection is respectfully traversed.

Jordan et al. shows that iron oxide particles can generate heat in a magnetic field at certain frequencies and magnetic fields. They further describe the method as a tool for heating whole tissue and killing cells by means of heat induced cell death (apoptosis or lysis), for use as a heating method in hyperthermia. Pope et al. describes an effective heat shock transformation process for *E. coli*.

However, the references, taken alone or in combination, do not teach or suggest the subject matter of the present claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

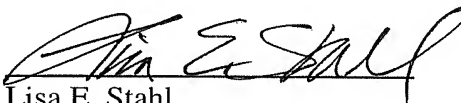
In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this Amendment and Reply, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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